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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/809,029	BARNARDO ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-17,20 and 22-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-17,20 and 22-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/24/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The Request for Continued Examination filed April 19, 2005 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-7 and 9-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 the recitation "wherein said one or more specific antibodies are each specific for a particular MHC allele" is vague and indefinite because is it unclear what relationship exists between the recombinant MCH molecule and the antibodies. Are the antibodies specific to a particular allele which is comprised in the recombinant MHC molecule or are the antibodies specific to MHC alleles of another molecule. Do these antibodies bind to the recombinant MHC allele. The one or more specific antibodies as recited does not refer back to the recombinant MHC molecule. Please clarify. See also deficiencies found in claim 2.

Claim 1 the recitation "wherein said one or more specific antibodies are each specific for a particular HMC allele" is vague and indefinite because it is unclear if each specific antibody binds different alleles or if the antibodies are produced against

different alleles. Further, it is unclear what characteristic in the MHC allele would cause it to bind. Please clarify. See also deficiencies found in claim 2.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-7, 14, 15 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Walter et al., (Stimulation of human cytotoxic T cells with HIV-1-derived peptides presented by recombinant HLA-A2 peptide complexes, International Immunology, vol. 9, No. 3, pp. 451-459, 1997).

Walter et al., disclose detecting a monoclonal W6/32 antibodies (specific for HLA-A,B,C (MHC class I molecules). Walter et al disclose that this antibody binds to recombinant HLA-A2 peptide complexes. Walter et al disclose detecting the W6/32 antibodies bound to the A2 complex with goat anti-mouse Ig conjugated to horseradish peroxidase (p. 452). Walter et al disclose that the HLA-A2 molecule is produced in E.Coli (prokaryotic expression system) (p. 451).

With respect to the recitation the presence of one or more specific anti-MHC antibodies as recited in the instant claims. Since Walter et al disclose detecting W6/32

antibody which is specific for HLA-A,B,C (HLA class I molecules), Walter et al teaches detecting an antibody specific for a specific HLA molecule.

5. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Viken et al. (Influence on Antibody Recognition of Amino Acid Substitutions in the cleft of HLA-DQ2 Molecules; Suggestive Evidence of Peptide-Dependent Epitopes," Human Immunology, Vol. 44, 1995, pp. 63-69).

Viken et al disclose detecting antibody reactivity with samples of antibodies to HLA-DQ2 Molecules which have been transfected (recombinant molecules). Viken et al disclose the use of secondary antibodies (page 64, column 2).

6. Claims 1-3 are rejected under 35 U.S.C. 102(e) as being anticipated by Carosella et al (US 6,528,304).

Carosella et al disclose immunoprecitating an K562-HLA-G2 cell (recombinant HLA) with a monoclonal antibody W6/32 (an antibody against MHC Class I heavy chains (anti HLA-A molecule). Carosella et al disclose detecting the monoclonal antibody with a labeled antibody (col 5, line 66 – col 6 line 25).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-7, 9-17, 20 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al (US 5,270,169) in view of Walter et al., (Stimulation of human cytotoxic T cells with HIV-1-derived peptides presented by recombinant HLA-A2 peptide complexes, International Immunology, vol. 9, No. 3, pp. 451-459, 1997).

Chang et al disclose detecting the presence of anti-HLA antibodies. Chang et al disclose combining HLA antigens with a biological sample to form a complex (col 2, lines 1-11, col 3, lines 47-64). Chang et al disclose that the HLA antigen may be a synthetic HLA antigen (col 3, lines 60-63). Chang et al disclose attaching the molecules

to a solid support such as a microtiter plate, beads or nitrocellulose (col 3, lines 1-19). Chang et al disclose that any convenient, accurate method may be employed for the detection of the surface bound complexes (col 4). Chang et al disclose comprising the reagents and components into a kit (col 5).

Chang et al differ from the instant invention in failing to specifically teach the HLA antigen is a recombinant HLA antigen.

Walter et al., disclose detecting a monoclonal W6/32 antibodies (specific for HLA-A,B,C (MHC class I molecules). Walter et al disclose that this antibody binds to recombinant HLA-A2 peptide complexes. Walter et al disclose detecting the W6/32 antibodies bound to the A2 complex with goat anti-mouse Ig conjugated to horseradish peroxidase (p. 452). Walter et al disclose that the HLA-A2 molecule is produced in E.Coli (prokaryotic expression system) (p. 451). Walter et al disclose the recombinant molecule can be immobilized and bound by antibody (p. 456, first column, lines 43 – 53).

It would have been obvious to one of ordinary skill in the art to incorporate a recombinant HLA antigen and the corresponding reagents as taught by Walter et al into the method of Chang et al because Chang et al teaches that the HLA antigen can be a synthetic HLA antigen and Walter shows that recombinant HLA antigens can be used to detect antibodies and one of ordinary skill would have a reasonable expectation of success incorporating recombinant HLA antigens as taught by Walter et al into the method of Chang.

11. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carosella et al (US 6,528,304) in view of Boguslaski et al (US 5,420,016).

See above for teachings of Carosella et al.

Carosella et al differ from the instant invention in failing to teach packaging the components into a kit.

Boguslaski et al disclose assembling various system components into a test kit. By assembling these components into test kits, it makes it more convenient and facile for the test operator (col 7. lines 8-11).

It would have been obvious to one or ordinary skill in the art to package the reagents and components as taught by Carosella et al into a kit because Boguslaski et al teaches that by assembling components into test kits, it makes it more convenient and facile for the test operator.

12. Claims 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al in view of Walter et al as applied to claims 1-7, 9-17, 20 and 22-24 above, and further in view of Luxembourg et al.

See above for teachings of Chang et al and Walter et al.

Chang et al and Walter et al differ from the instant invention in failing to teach the MHC or HLA molecule is fused to biotin.

Luxembourg et al disclose recombinant MHC molecules which are biotinylated (page 3, paragraph 0018, & page 4, paragraph 0027). Luxembourg et al disclose that these recombinant MHC molecules are biotinlyated to provide attachment to solid support coated with avidin. Luxemburg et al disclose that the use of this avidin-biotin

system provides for the isolation of peptides such as antibodies (p. 5, paragraphs 0030, and 0031).

It would have been obvious to one of ordinary skill in the art to incorporate an avidin-biotin system as taught by Luxembourg et al into the modified method of Chang et al because Luxembourg et al shows that the use of this avidin-biotin system provides for the isolation of peptides such as antibodies. Further, the use of avidin-biotin systems to immobilize and capture reagents is very well known in the art. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating avidin-biotin as taught by Luxembourg et al into the modified method of Chang et al.

Response to Arguments

13. Applicant's arguments filed 03/21/05 have been fully considered but they are not persuasive.

Applicant argues that the amended claims are one which specifically recognize a single, particular molecule within a class of MHC (or HLA) molecules rather than simply the class of MHC (or HLA) molecules, respectively as taught in the prior art. Applicant argues that the cited references only disclose antibodies which recognize a single class of molecule, and cannot further differentiate and recognize a single, particular molecule within the class, the references do not anticipate the cited claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., one which specifically recognize a single, particular molecule within a class of MHC (or HLA)

molecules rather than simply the class of MHC (or HLA molecues)) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, as stated above it is unclear what applicant intends by the amendment "wherein, said one or more specific antibodies are each specific for a particular MHC allele" (see 112 2nd rejections above). Accordingly, the prior art references read on the instantly recited claims.

Applicant argues that there is no motivation to combine Chang et al and Walter et al. Applicant stated that Applicants have noted in responding to a previous office action, there has been a resistance in the prior art to the use or recombinant molecules because of their presumed inability to retain their natural epitopic integrity. This is not found persuasive because after reviewing Applicants arguments filed 01/16/03 (which was the only arguments examiner could find directed to this issue in the prosecution of this application). That argument stated that (see page 10-11 or remarks section filed 01/16/03). "Prior to the present invention, the prior art relied exclusively on the use of naturally isolated MHC or HLA molecules for methods MHC or HLA antibody detection. No prior art of which Applicants are aware used recombinant MHC or HLA molecules for detecting anti-MHC antibodies or anti-HLA antibodies, respectively. Although recombinant MHC/HLA molecules have been generated previously, they have been used only in t-cell assays. T cells utilize a different epitope on the MHC or HLA molecules in comparison to antibodies, and t-cell binding is very dependent on the peptides loaded into the groove of the MHC or HLA molecule. The T-cell receptor of a

particular cell is absolutely specific for a unique peptide/MHC or unique peptide/HLA combination. Thus, recombinant molecules which present that peptide are compatible with T-cell assay. In contrast, MHC/HLA antibodies are not directed to the peptide and bind to the HMC/HLA molecule itself. Thus, only molecules retaining absolute epitopic integrity could be used and it was assumed that this could be found only in naturally occurring molecules". This is not found persuasive because as the prior art used in this rejection indicates, it was known in the art to use recombinant HLA molecules in the detection of antibodies and as stated above Chang specifically teaches that synthetic molecules can be used and Walter specifically teaches the use of recombinant molecules (which are synthetically produced) to detect antibodies. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating recombinant molecules and reagents as taught by Walter et al into the method of Chang et al.

Applicant argues that in view of the concern in the prior art regarding the use of recombinant antibodies, there is question as to what Chang et al. were advocating when referring to synthetic HLA antigens. This is not found persuasive because it is not on point. The instant claims are directed to recombinant HMC molecules and not recombinant antibodies and thus it is unclear what Applicant is arguing.

Applicant argues that Walter et al. teaches that W6/32 binds recombinant HLA antigens. However, this antibody is well known to be directed to a monomorphic region of the antigen present in class I antigens. Retention of this epitope in recombinant molecules would not lead the skilled person to believe that polymorphic epitopes would

be retained in recombinant molecules. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., polymorphic epitopes would be retained in recombinant molecules) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

14. NOTE: it is noted that applicant did not amend claim 20 directed toward a kit. Therefore, the additional rejection of claim 20 under Carosella et al (US 6,528,304) in view of Boguslaski et al (US 5,420,016) is applied above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts

Gary Counts
Examiner
Art Unit 1641
June 6, 2005

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06/10/05